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EXAMINER	
DOE, SHANTA G	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,249	LEDUC ET AL.	
	Examiner	Art Unit	
	SHANTA G. DOE	1775	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22-47,49-72,74-86,88-99,101-122,124-143 and 145-157* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13-18,31,40-45,56-72,74-86,88-99, 101-122, 124-131, 133 and 135* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2-12,19,20,22-30,32-39,46,47,49-55,132,134,136-143 and 145-157.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments with respect to newly amended claims 1, 31, 56, 86, 111 and their dependent claims have been considered but are moot in view of the new ground(s) of rejection. See art rejection below.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 31, 86 and their dependent claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitation stating " an elastomeric growth substrate comprising an elastomeric membrane of a first material, defining a three-dimensional cell strain surface having an elasticity differential that comprises one of(i) an elastic modulus differential between a first portion and a second portion of the first material and (ii) a surface feature differential between the first and second portions, " was not described in the specification in such a way to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification discloses a growth substrate comprising an elastomeric membrane of first material comprising a first portion having a first elasticity and a second portion having a second elasticity but the specification fails to provide support for "an elastomeric growth substrate comprising an elastomeric membrane of a first material, ***defining a three-dimensional cell strain surface having an elasticity differential that comprises one of(i) an elastic modulus differential between a first portion and a second portion of the first material and (ii) a surface feature differential between the first and second portions***"

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banes (US 6,048,723) in view of Pishko et al (US 2003/0175824) and Desai et al (WO2004/046337).

Regarding claims 1 and 31, Banes discloses a cell growth apparatus (see fig 18-20) comprising a cell growth chamber (called well 815) having an interior side and an exterior side and comprising a wall (called cylindrical body 805) and a base (870) defining an interior volume, the cell growth chamber comprising an elastomeric growth substrate (membrane 840 or 200 covered with a three-dimensional flexible growth substrate) comprising an elastomeric membrane of a first material defining a three-dimensional cell strain surface having an elasticity differential that comprises one of(i) an elastic modulus differential between a first portion and a second portion of the first material (there is an elastic modulus differential between the portion coated with the

three-dimensional growth and the portion that is not) and (ii) a surface feature differential between the first and second portions (the bottom surface has a different elasticity than the top surface that has been covered with three-dimensional flexible growth substrate, see col. 5 lines 27-53) (see fig 1A, 18-20; abs, col. 5 lines 27-53, col. 9 lines 55-col. 10 lines 35). However, Banes fails to disclose that the elastomeric membrane have one or more engineered structural formations integrated therewith for receiving and growing cells.

Pishko et al (US 2003/0175824) discloses system comprising a three-dimensional hydrogel microstructure (such micro-fluidic network comprising a micro-channel) for cell growth on a flexible substrate (see [0023] & [0037]) such as rubber or plastic or silicon) or on a glass substrate (Pishko abs, [0008]-[0017], [0036], [0037],[0039], [0043], [0047] ,[0048] and entire document)

Desai et al (WO2004/046337) discloses that it is known in the art for cell growth substrate to comprise engineered structural formation such as groove and/or passageway (called micro-channel (see page 5 lines 26-28) within the membrane/substrate/layer within the growth substrate (see fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

In view of Pishko and Desai, it would have been obvious to one having ordinary skill in the art at the time of the invention to have growth substrate further comprise engineered structural formation such as a surface groove and a passageway within the membrane/layer of the substrate as is taught by Pishko and Desai, since such a

modification would enable the transport of substance (such as nutrient or test chemical such as drugs) to the layer/membrane.

5. Claims 1, 13, 14, 16, 31, 40, 41,43, 56-64, 66, 67, 69, 71, 72, 74-78, 83, 85, 86, 88-91, 93, 94, 96, 98, 99, 101-105, 110, 111, 112, 117-122, 124, 125, 130, 131 and 133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banes (WO02/46365) in view of Pishko et al (US 2003/0175824) and Desai et al (WO2004/046337).

Regarding claims 1 and 31, Banes discloses a cell growth apparatus (see fig. 3) comprising a cell growth chamber (called culture well (42)) having an interior side and an exterior side and comprising a wall and a base(see fig 3) defining an interior volume, the cell growth chamber comprising an elastomeric growth substrate (flexible membrane (12) is covered with a three-dimensional flexible growth substrate) comprising an elastomeric membrane of a first material defining a three-dimensional cell strain surface having an elasticity differential that comprises one of(i) an elastic modulus differential between a first portion and a second portion of the first material (there is a modulus differential between the portion coated with the three-dimensional growth and the portion that is not) and (ii) a surface feature differential between the first and second portions (the bottom surface has a different elasticity than the top surface that has been treated/coated with gel matrix; see page 9 lines 8 -19)) (see fig. 1, 3 and 10; abs; page 5 lines 18-28, page 9 lines 8 -19 and entire document). However, Banes fails to disclose

that the elastomeric membrane have one or more engineered structural formations integrated therewith for receiving and growing cells.

Pishko et al (US 2003/0175824) discloses system comprising a three-dimensional hydrogel microstructure (such micro-fluidic network comprising a micro-channel) for cell growth on a flexible substrate (see [0023] & [0037]) such as rubber or plastic or silicon) or on a glass substrate (Pishko abs, [0008]-[0017], [0036], [0037],[0039], [0043], [0047] ,[0048] and entire document)

Desai et al (WO2004/046337) discloses that it is known in the art for cell growth substrate to comprise engineered structural formation such as groove and/or passageway (called micro-channel (see page 5 lines 26-28) within the membrane/substrate/layer within the growth substrate (see fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

In view of Pishko and Desai, it would have been obvious to one having ordinary skill in the art at the time of the invention to have growth substrate further comprise engineered structural formation such as a surface groove and a passageway within the membrane/layer of the substrate as is taught by Pishko and Desai, since such a modification would enable the transport of substance (such as nutrient or test chemical such as drugs) to the layer/membrane.

Regarding claim 13, the combination as applied to claim 1 above discloses the apparatus of claim 1 wherein the interior side (22) of the elastomeric membrane is

partially or fully coated with an extracellular matrix-mimetic (called gel matrix) (see Banes page 9 lines 11-19).

Regarding claim 14, the combination as applied to claim 13 above discloses the apparatus of claim 13, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-eo-glycolide) and a self-complementary oligopeptide matrix (see Banes page 9 lines15 - 19).

Regarding claim 16, the combination as applied to claim 13 above discloses the apparatus of claim 13, wherein the extracellular matrix mimetic partially coats the interior side (top side/surface having 14 attached thereto) of the elastomeric membrane (12)(the examiner believe that the surface 22 is partially coated with the matrix because part of the membrane have anchor (14) attached thereto(see fig 10)), so gel matrix would be applied to the part of the membrane 12 between the two anchor 14, the specification does not disclose the gel matrix is applied to the anchor) (see Banes fig 3 and 10; abs; page 9 lines 11-19 and entire document) .

Regarding claim 40, the combination as applied to claim 31 above discloses the substrate of claim 31, wherein the interior side of the elastomeric membrane is partially or fully coated with an extracellular matrix-mimetic(called gel matrix) (see Banes page 9 lines 11-19).

Regarding claim 41, the combination as applied to claim 40 above discloses the substrate of claim 40, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix(see Banes page 9 lines15 - 19).

Regarding claim 43, the combination as applied to claim 40 above discloses the substrate of claim 40, wherein the extracellular matrix mimetic partially coats the interior side of the elastomeric membrane)(the examiner believe that the surface 22 is partially coated with the matrix because part of the membrane has anchor (14) attached thereto (see fig 10)), so gel matrix would be applied to the part of the membrane 12 between the two anchors 14, the specification does not disclose the gel matrix is applied to the anchor) (see Banes fig 3 and 10; abs; page 9 lines 11-19 and entire document).

Regarding claim 56, Banes discloses a cell growth apparatus (10) comprising a cell growth chamber (called well 42) having an interior side and an exterior side and comprising a wall and a base defining an interior volume (see fig 1, 3 and 10), the cell growth chamber (well 42) comprising an elastomeric growth substrate comprising an elastomeric membrane (flexible membrane (12)) of a first material having an interior side and an exterior side, wherein the elastomeric membrane is at least partially coated with an extracellular matrix-mimetic (called gel matrix) (the top surface is treated/coated

with gel matrix; see Banes page 9 lines 8 -19)) (see Banes fig. 1, 3 and 10; abs; page 5 lines 18-28, page 9 lines 8 -19 and entire document). However, Banes fails to disclose that the elastomeric membrane have one or more engineered structural formations integrated therewith for receiving and growing cells.

Pishko et al (US 2003/0175824) discloses system comprising a three-dimensional hydrogel microstructure (such micro-fluidic network comprising a micro-channel) for cell growth on a flexible substrate (see [0023] & [0037]) such as rubber or plastic or silicon) or on a glass substrate (Pishko abs, [0008]-[0017], [0036], [0037],[0039], [0043], [0047] ,[0048] and entire document)

Desai et al (WO2004/046337) discloses that it is known in the art for cell growth substrate to comprise engineered structural formation such as groove and/or passageway (called micro-channel (see page 5 lines 26-28) within the membrane/substrate/layer within the growth substrate (see fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

In view of Pishko and Desai, it would have been obvious to one having ordinary skill in the art at the time of the invention to have growth substrate further comprise engineered structural formation such as a surface groove and a passageway within the membrane/layer of the substrate as is taught by Pishko and Desai, since such a modification would enable the transport of substance (such as nutrient or test chemical such as drugs) to the layer/membrane.

Regarding claim 57, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein the membrane comprises a first portion having a first elasticity and a second portion having a second elasticity(the bottom surface has a different elasticity than the top surface that has been treated/coated with gel matrix, in addition the part of the membrane that has the anchor (14) attached would have a different elasticity than the part of the membrane that don't; see Banes page 9 lines 8 - 19) (see Banes fig 1,3, and 10; abs; page 9 lines 8 -19 and entire document) .

Regarding 58, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein at least a portion of the base of the cell growth chamber consists of the elastomeric growth substrate (see Banes page 5 lines 21 -26)

Regarding claim 59, the combination as applied to claim 58 above discloses the apparatus of claim 58, further comprising a secondary chamber (called trough (46)) in fluid connection with and partially defined by an exterior side of the elastomeric growth substrate, the secondary chamber comprising an opening having a fitting for a pipe or tube (see Banes fig 3 and 10 and page 7 lines 22-30).

Regarding claim 60, the combination as applied to claim 59 above discloses the apparatus of claim 59, further comprising a pump in fluid communication with the secondary chamber (Vacuum source (54)) (see Banes fig 3 and page 7 lines 22-30).

Regarding claim 61, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein the elastomeric membrane has a portion of a first thickness, having a first elasticity, and a portion of a second thickness, having a second elasticity (the elastomeric membrane has a portion with first thickness which comprising the part of the membrane between the two anchor 14 and portion of second thickness comprises of the membrane (12) and the anchor (14) that has been attached to the membrane see fig 3 and 10) (see Banes fig 3 and 10; abs and entire document).

Regarding claim 62, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein a second material (the anchor (14) may be constructed from material such as nylon or silk wherein the material may be solid or mesh) having a different elasticity than the first material (material from which the flexible membrane (12) is made) is embedded within or attached to the elastomeric membrane (see Banes page 5 line 30 –page 6 line 25).

Regarding claim 63, the combination as applied to claim 62 above discloses the apparatus of claim 62, wherein the second material is one of a polymer; a metal, a ceramic and a fabric (see Banes page 6 lines 23-25).

Regarding claim 64, the combination as applied to claim 63 above discloses the

apparatus of claim 63, wherein the second material is nylon mesh (see Banes page 6 lines 23-25).

Regarding claim 66, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein the substrate further comprises one or more additional elastomeric layers, at least one of which is attached to the elastomeric membrane(the layer of collagen gel that is coated on the elastomeric material is elastomeric)(see Banes page 9 lines15 -19).

Regarding claim 67, the combination as applied to claim 66 above discloses the apparatus of claim 66, wherein one or more of the additional elastomeric layer is biodegradable (the collagen gel layer is biodegradable).

Regarding claim 69, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-co-glycolide) and a self-complementary oligopepfide matrix (see Banes page 9 lines15 -19).

Regarding claim 71, the combination as applied to claim 56 above discloses that the apparatus of claim 56 wherein the first portion has a first elastic modulus and the

second portion has a second elastic modulus (it is inherent that if the different portions have different elasticity that the elastic modulus would be different as well).

Regarding claim 72, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein the membrane comprises one or more internal passageways (medium flow through the membrane which implies that there has to be a passageway for the liquid to flow through) (see Banes page 12 line 30 – page 13 line 1).

Regarding claims 74, 101, and 124, the combination as applied to claims 56, 86 and/or 111 discloses the apparatus of claims 56, 86 and/or 111 wherein the engineered structural formation is one of a surface groove and a passageway within the membrane (see Desai et al fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

Regarding claims 75, 102, and 125, the combination as applied to claims 74, 101 and 124 above discloses the apparatus of claims 74, 101 and 124 having microchannels. The combination fails to disclose that the surface groove or passageway (microchannel) within the membrane has a diameter of less than 100μ.

However, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the surface groove or passageway (microchannel) have a diameter of less than 100μ, since it has been held that where the general conditions of a

claim are disclose in the prior art, discovering the optimum or workable ranges involves only routine skill in the art.

Regarding claims 76, and 103, the combination as applied to claims 75, and 101 above discloses the apparatus of claims 75, and 101, wherein the membrane/substrate comprises an internal passageway (called micro channel) that opens into the interior volume(see entire document especially page 20, page 25).

Regarding claims 77 and 104, the combination as applied to claim 76 and 103 above discloses the apparatus of claim 76, wherein the passageway is coated with an extracellular matrix mimetic (see Desai et al page 20 lines 8 -11, page 25).

Regarding claim 78, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein the extracellular matrix mimetic partially coats the interior side of the elastomeric membrane (the examiner believes that the surface 22 is partially coated with the matrix because part of the membrane have anchors (14) attached thereto(see fig (10)), so gel matrix would be applied to the part of the membrane 12 between the two anchors 14, the specification does not disclose that the gel matrix is applied to the anchor) (see Banes fig 3 and 10; abs; page 9 lines 11-19 and entire document).

Regarding claim 83, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein the wall is annular (see Banes fig. 1).

Regarding claim 85, the combination as applied to claim 56 above discloses the apparatus of claim 56, wherein at least a portion of the substrate is coated with an adhesion promoter (collagen coated on the membrane (12)) (see Banes page 9 lines 11-19 and entire document).

Regarding claim 86, Banes discloses a cell growth substrate, comprising an elastomeric membrane (12) of a first material that is at least partially coated with an extracellular matrix-mimetic, the elastomeric membrane comprising an elastomeric membrane of a first material defining a three-dimensional cell strain surface having an elasticity differential that comprises one of(i) an elastic modulus differential between a first portion and a second portion of the first material (there is a modulus differential between the portion coated with the three-dimensional growth and the portion that is not) and (ii) a surface feature differential between the first and second portions (the bottom surface has a different elasticity than the top surface that has been treated/coated with gel matrix; see Banes page 9 lines 8 -19)) (the top surface is treated/coated with gel matrix; see Banes page 9 lines 8 -19)) (see Banes fig. 1, 3 and 10; abs; page 5 lines 18-28, page 9 lines 8-19 and entire document). However, Banes fails to disclose that the

elastomeric membrane have one or more engineered structural formations integrated therewith for receiving and growing cells.

Pishko et al (US 2003/0175824) discloses system comprising a three-dimensional hydrogel microstructure (such micro-fluidic network comprising a micro-channel) for cell growth on a flexible substrate (see [0023] & [0037]) such as rubber or plastic or silicon) or on a glass substrate (Pishko abs, [0008]-[0017], [0036], [0037],[0039], [0043], [0047] ,[0048] and entire document)

Desai et al (WO2004/046337) discloses that it is known in the art for cell growth substrate to comprise engineered structural formation such as groove and/or passageway (called micro-channel (see page 5 lines 26-28) within the membrane/substrate/layer within the growth substrate (see fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

In view of Pishko and Desai, it would have been obvious to one having ordinary skill in the art at the time of the invention to have growth substrate further comprise engineered structural formation such as a surface groove and a passageway within the membrane/layer of the substrate as is taught by Pishko and Desai, since such a modification would enable the transport of substance (such as nutrient or test chemical such as drugs) to the layer/membrane.

Regarding claim 88, the combination as applied to claim 86 above discloses the substrate of claim 86, wherein the elastomeric membrane has a portion of a first

thickness, having a first elasticity, and a portion of a second thickness, having a second elasticity (the elastomeric membrane has a portion with first thickness which comprising the part of the membrane between the two anchors 14 and portion of second thickness comprises of the membrane (12) and the anchor (14) that has been attached to the membrane where in the elasticity in each portion differ see fig 3 and 10) (see Banes fig 3 and 10; abs and entire document) .

Regarding claim 89, the combination as applied to claim 86 above discloses the substrate of claim 86, wherein a second material (the anchor (14) may be constructed from material such as nylon or silk wherein the material may be solid or mesh) having a different elasticity than the first material (material from which the flexible membrane (12) is made) is embedded within or attached to the elastomeric membrane (see Banes page 5 line 30 –page 6 line 25)

Regarding claim 90, the combination as applied to claim 89 above discloses the substrate of claim 89, wherein the second material is one of a polymer; a metal, a ceramic and a fabric (see Banes page 6 lines 23-25).

Regarding claim 91, the combination as applied to claim 90 above discloses the apparatus of claim 90, wherein the second material is nylon mesh (see Banes page 6 lines 23-25).

Regarding claim 93, the combination as applied to claim 86 above discloses the substrate of claim 86, wherein the substrate further comprises one or more additional elastomeric layers (the substrate is coated with collagen), at least one of which is attached to the elastomeric membrane (see Banes page 9 lines15 -19).

Regarding claim 94, the combination as applied to claim 93 above discloses the substrate of claim 93, wherein one or more of the additional elastomeric layer is biodegradable (the collagen gel layer is biodegradable) (see Banes page 9 lines15 - 19)).

Regarding claim 96, the combination as applied to claim 86 above discloses the substrate of claim 86, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide-co-glycolide) and a self-complementary oligopeptide matrix(see page Banes 9 lines15 - 19).

Regarding claim 98, the combination as applied to claim 86 above discloses the substrate of claim 86, wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus(the bottom surface has a different elasticity/elastic modulus than the top surface that has been treated/coated with gel matrix, in addition the part of the membrane that has the anchor (14) attached would

have a different elasticity than the part of the membrane that don't; see Banes page 9 lines 8 -19) (see Banes fig 1,3, and 10; abs; page 9 lines 8 -19 and entire document).

Regarding claim 99, the combination as applied to claim 86 above discloses the substrate of claim 86, wherein the membrane comprises one or more internal passageways (medium flow through the membrane which implies that there has to be a passageway for the liquid to flow through) (see Banes page 12 line 30 – page 13 line 1).

Regarding claim 105, the combination as applied to claim 86 above discloses the substrate of claim 86, wherein the extracellular matrix mimetic partially coats the interior side of the elastomeric membrane(the examiner believe that the surface 22 is partially coated with the matrix because part of the membrane have anchor (14) attached thereto(see fig (10)), so gel matrix would be applied to the part of the membrane 12 between the two anchor 14, the specification does not disclose that the gel matrix is applied to the anchor) (see Banes fig 3 and 10; abs; page 9 lines 11-19 and entire document).

Regarding claim 110, the combination as applied to claim 86 above discloses the apparatus of claim 86, wherein at least a portion of the substrate is coated with an adhesion promoter (collagen gel)(see Banes page 9 lines 11-19).

Regarding claim 111, Banes discloses a method of producing an elastomeric cell

growth substrate, comprising coating at least a portion of an elastomeric membrane with an extracellular matrix mimetic (the examiner believes that the surface 22 is partially coated with the matrix (collagen) because part of the membrane has anchors (14) attached thereto(see fig (10)), so gel matrix would be applied to the part of the membrane 12 between the two anchors 14, the specification does not disclose that the gel matrix is applied to the anchor) (see Banes fig 3 and 10; abs; page 9 lines 11-19 and entire document). However, Banes fails to disclose that the elastomeric membrane has one or more engineered structural formations integrated there within.

Pishko et al (US 2003/0175824) discloses system comprising a three-dimensional hydrogel microstructure (such micro-fluidic network comprising a micro-channel) for cell growth on a flexible substrate (see [0023] & [0037]) such as rubber or plastic or silicon) or on a glass substrate (see Pishko abs, [0008]-[0017], [0036], [0037],[0039], [0043], [0047] ,[0048] and entire document).

Desai et al (WO2004/046337) discloses that it is known in the art for cell growth substrate to comprise engineered structural formation such as groove and/or passageway (called micro-channel (see page 5 lines 26-28) within the membrane/substrate/layer within the growth substrate (see Desai fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

In view of Pishko and Desai, it would have been obvious to one having ordinary skill in the art at the time of the invention to have growth substrate further comprise engineered structural formation such as a surface groove and a passageway within the

membrane/layer of the substrate as is taught by Pishko and Desai, since such a modification would enable the transport of substance (such as nutrient or test chemical such as drugs) to the layer/membrane.

Regarding claim 112, the combination as applied to claim 111 above discloses the method of claim 111, wherein the extracellular matrix mimetic is selected from the group consisting of fibronectin, vitronectin, collagen, laminin, poly(lactide), poly(lactide- co-glycolide) and a self-complementary oligopeptide matrix (see Banes page 9 lines 11-19).

Regarding claim 117, the combination as applied to claim 111 above discloses the method of claim 111, wherein the membrane has a first portion having a first elasticity and a second portion having a second elasticity(the bottom surface has a different elasticity/elastic modulus than the top surface that has been treated/coated with gel matrix, in addition the part of the membrane that has the anchor (14) attached would have a different elasticity than the part of the membrane that don't; see Banes page 9 lines 8 -19) (see Banes fig 1,3, and 10; abs; page 9 lines 8 -19 and entire document).

Regarding claim 118, the combination as applied to claim 117 above discloses the method of claim 117, wherein the first portion has a first elastic modulus and the second portion has a second elastic modulus (it is inherent that if the different portions have different elasticity that the elastic modulus would be different as well).

Regarding claim 119, the combination as applied to claim 117 above discloses the method of claim 117, wherein the membrane has portion differing thickness (the elastomeric membrane has a portion with first thickness which comprising the part of the membrane between the two anchors 14 and portion of second thickness comprises of the membrane (12) and the anchor (14) that has been attached to the membrane see fig 3 and 10) (see Banes fig 3 and 10; abs and entire document)

Regarding claim 120, the combination as applied to claim 117 above discloses the method of claim 117, wherein a material of a different elastic modulus (the anchor (14) may be constructed from material such as nylon or silk wherein the material may be solid or mesh which has a different elastic modulus than the flexible membrane (12) to which it is attached) than that of the membrane is embedded within or attached to the membrane (see Banes page 5 line 30 –page 6 line 25)

Regarding claim 121, the combination as applied to claim 120 above discloses the method of claim 120, wherein the material is one of a nylon mesh and a stainless steel mesh (the anchor (14) may be constructed from material such as nylon or silk wherein the material may be solid or mesh) (see Banes page 5 line 30 –page 6 line 25).

Regarding claim 122, the combination as applied to claim 117 above discloses the method of claim 117, wherein the membrane comprises one or more internal

passageways (medium flow through the membrane which implies that there has to be a passageway for the liquid to flow through) (see Banes page 12 line 30 – page 13 line 1).

Regarding claim 130, the combination as applied to claim 111 above discloses the method of claim 111, wherein a second elastomeric layer (collagen gel layer) is attached to the membrane.

Regarding claim 131, the combination as applied to claim 130 discloses the method of claim 130 wherein the engineered structural formation is a groove and the second elastomeric layer is aligned over the groove to form a passageway (see Desai fig 1 and 4) (see Banes fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

Regarding claim 133, Banes discloses the method of producing an elastomeric growth substrate comprising preparing an elastomeric membrane of first material that comprises a first portion having a first elasticity and a second portion having a second elasticity, and further comprising coating at least a portion of the elastomeric membrane with an extracellular matrix mimetic (the bottom surface has a different elasticity/elastic modulus than the top surface that has been treated/coated with gel matrix, in addition the part of the membrane that has the anchor (14) attached would have a different elasticity than the part of the membrane that don't; see page 9 lines 8 - 19) (see Banes fig 1,3, and 10; abs; page 9 lines 8 -19 and entire document). However,

Banes fails to disclose that the elastomeric membrane has one or more engineered structural formations integrated there within.

Pishko et al (US 2003/0175824) discloses system comprising a three-dimensional hydrogel microstructure (such micro-fluidic network comprising a micro-channel) for cell growth on a flexible substrate (see [0023] & [0037]) such as rubber or plastic or silicon) or on a glass substrate (see Pishko abs, [0008]-[0017], [0036], [0037],[0039], [0043], [0047] ,[0048] and entire document).

Desai et al (WO2004/046337) discloses that it is known in the art for cell growth substrate to comprise engineered structural formation such as groove and/or passageway (called micro-channel (see page 5 lines 26-28) within the membrane/substrate/layer within the growth substrate (see Desai fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 and entire document).

In view of Pishko and Desai, it would have been obvious to one having ordinary skill in the art at the time of the invention to have growth substrate further comprise engineered structural formation such as a surface groove and a passageway within the membrane/layer of the substrate as is taught by Pishko and Desai, since such a modification would enable the transport of substance (such as nutrient or test chemical such as drugs) to the layer/membrane.

6. Claims 15, 42, 68, 70, 81, 82, 95, 97, 108, 109, 113, and 135 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banes (WO02/46365) in view of Pishko et al (US 2003/0175824) and Desai et al (WO2004/046337) as applied to the claims above and further in view of Takezawa et al (US 2002/0164796).

Regarding claims 15, 42, 70, 97, 113 and 135, the combination as applied to claims 13, 40, 69, 96, 111 and 133 to disclose the device/method of claims 13, 40, 69, 96, 111 and 133. However, the combination fails to specifically disclose that the extracellular matrix mimetic is fibronectin.

Takezawa et al (US 2002/0164796) discloses that it is known in the art to have carrier for cell culture comprising material coated (layer to coat support) with extracellular matrix such as collagen or fibronectin (see Takezawa [003]).

In view of Takezawa, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the cell growth substrate (same as carrier of cell culture) be coated with fibronectin instead of collagen since Takezawa discloses that fibronectin is a functionally equivalent extracellular matrix mimetic known in the art (to coated a support/substrate use for cell growth).

Regarding claims 81 and 108, the combination as applied to claims 56 and/or 86 discloses the apparatus of claims 56 and /or 86. The combination fails to specifically disclose that the elastomeric membrane is biodegradable.

Takezawa et al. (US 2002/0164796) discloses that it is known in the art to have carrier for cell culture comprising material which are biodegradable (see Takezawa [003]).

In view of Takezawa, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the elastomeric membrane of the growth substrate/support be biodegradable as is taught by Takezawa, since, it has been held to be within the general skill of a worker in the art to select a known material on the basis of it suitability for the intended use as a matter of obvious design choice.

Regarding claims 68, 82, 95, and 109, the combination as applied to claims 67, 81, 94 and /or 108 discloses the apparatus/method of claims 67, 81, 94 and/or 108. The combination fails to specifically disclose that the biodegradable layer comprises a poly (glycerol-sebaeate) polymer.

However, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the biodegradable layer comprise a poly (glycerol-sebaeate) polymer, since it has be held to be within the general skill of a worker in the art to select a known material on the basis of it suitability for the intended use a matter of obvious design choice.

7. Claims 17, 44, 79, 106, 114, 115 and 126-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banes (WO02/46365) in view of Pishko et al

(US 2003/0175824) and Desai et al (WO2004/046337) as applied to the claims above and further in view of Leduc P., et al., Use of Micropatterned Adhesive Surfaces for Control of Cell Behavior, Method in Cell Biology 69,pp395-401(2002).

Regarding claims 17, 44, 79, 106 and 114, the combination as applied to claims 16, 43, 78, 105, and/or 111 discloses the apparatus/method of claims 16, 43, 78, 105 and /or 111. The combination fails to disclose that the apparatus further comprising an adhesion inhibitor covering parts of the interior side of the elastomeric membrane not covered by the extracellular matrix mimetic.

Leduc discloses that it was know in the art to have a cell growth substrate comprising adhesion inhibitor (called polyethylene glycol (peg), see page 386) covering part of the substrate not covered by extracellular matrix mimetic (see entire Leduc document specifically page 386 and 389).

In view of Leduc, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the growth substrate of Banes further comprise an adhesion inhibitor covering parts growth substrate not covered by the extracellular matrix mimetic as is taught by Leduc since Leduc states that such a modification would ensure that the size and shape of the cells on the growth substrate are controlled (see Leduc page 386 and 389).

Regarding claim 115, the combination as applied to claim 114 above discloses the apparatus of claim 114. The combination fails to specifically disclose that the adhesion inhibitor is one of bovine serum albumin.

Desai et al (WO2004/046337) discloses that it is known in the art to coat part of a growth substrate with adhesion inhibitor such bovine serum albumin in order to inhibit cell adhesion in the said coated portion (see Desai, page 18 lines 23-25).

In view of Desai, it would have been obvious to one having ordinary skill in the art at the time of the invention to replace the adhesion inhibitor of the combined references with the known adhesion inhibitor of bovine serum albumin as is taught by Desai, since, it is a functionally equivalent adhesion inhibitor known in the art.

Regarding claim 126, the combination as applied to claim 111 above discloses the method of claim 111. The combination fails to disclose that the membrane is prepared by curing an elastomeric polymer in a mold containing a form defining the engineered structural formation.

Desai et al (WO2004/046337) discloses that it is well known in the art to make a cell growth substrate/membrane by curing an elastomeric polymer such as PDMS into a mold whereby the PDMS constitutes microchannels (see Desai page 18 lines 10-20) within the membrane/substrate/layer of the growth substrate (see Desai fig 1, 2 and 4, page 3 lines 20 -30, page 4, page 5 lines 26-28, page 10 line 24 – page 11 line 2 , page 18 lines 10-20 and entire document).

Leduc discloses that it is known in the art to make a cell growth substrate by curing an elastomeric polymer such as PDMS into a mold whereby the PDMS constitutes form defining the engineered structural formation (called island) (see Leduc fig 2, page 388 and entire document)

In view of Desai or Leduc, it would have been obvious to one having ordinary skill in the art at the time of the invention to use the well known method of preparing the growth substrate/membrane by curing an elastomeric polymer into a mold containing a form defining the engineered structural formation as is taught by Desai or Leduc, since it is a functionally equivalent means/method well known in the for making growth substrate/membrane.

Regarding claim 127, the combination as applied to claim126 above discloses the method of claim 126 wherein the form defining the engineered structural formation is a silicon wafer comprising a patterned photoresist layer defining the engineered structural formation (see Leduc fig. 2, page 388 and Desai fig 2; page 17).

Regarding claim 128, the combination as applied to claim 126 above discloses the method of claim 126 comprising pouring PDMS over silicon wafer comprising a patterned photoresist layer defining the engineered structural formation and heal curing the PDMS(see Leduc fig. 2, page 388 and Desai fig 2; page 17).

Regarding claim 129, the combination as applied to claim 126 discloses the method of

claim 126, wherein the engineered structural formation is a channel (see Desai page 18 lines 10-20).

8. Claims 18, 45, 80, 107 and 116 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banes (WO02/46365) in view of Pishko et al (US 2003/0175824) and Desai et al (WO2004/046337) and Leduc P., et al., Use of Micropatterned Adhesive Surfaces for Control of Cell Behavior, Method in Cell Biology 69,pp395-401(2002) as applied to claims 17, 44, 79, 106 and 114 above, and further in view of Liu et al, Engineering protein and cell adhesivity using PEO-terminated triblock polymer, http://web.mit.edu/lmrt/publications/2002/Liu2002_JBMR.pdf , 2002 .

Regarding claims 18, 45, 80,107, and 116, the combination as applied to claims 17, 44, 79, 106 and 114 above discloses the apparatus of claims 17, 44, 79, 106 and 114. The combination fails to specifically disclose that the adhesion inhibitor is one of bovine serum albumin and a poly (ethylene oxide)/poly (propylene oxide)/poly (ethylene oxide) triblock polymer.

Liu discloses that it is known in the art to coat part of a growth substrate with adhesion inhibitor such as poly (ethylene oxide) triblock polymer in order to inhibit cell adhesion in the said coated portion (see Liu, abs and entire document).

In view of Liu, it would have been obvious to one having ordinary skill in the art at the time of the invention to replace the adhesion inhibitor of the combined references with the known adhesion inhibitor of poly(ethylene oxide) triblock polymer as is taught

by Liu since it is a functionally equivalent adhesion inhibitor known in the art.

9. Claims 65, 84, and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banes (WO02/46365) in view of Pishko et al (US 2003/0175824) and Desai et al (WO2004/046337) as applied to the claims above.

Regarding claims 65 and 92, the combination as applied to claims 63 and 90 discloses the apparatus of claims 63 and 90 comprising a mesh. The combination fails to disclose that the mesh is a stainless steel mesh.

However, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the mesh be a stainless steel mesh since, it has be held to be within the general skill of a worker in the art to select a known material on the basis of it suitability for the intended use a matter of obvious design choice

Regarding claim 84, the combination as applied to claim 56 discloses the apparatus of claim 56. The combination fails to specifically disclose that the wall is ellipsoid.

However, it would have been obvious to one having ordinary skill in the art at the time of the invention to have the wall of the Banes apparatus be ellipsoid because the wall being ellipsoid does not functionally distinguish the apparatus from what is being taught in the prior art (whether the wall of the growth chamber is ellipsoid or another shape does not change the function of the wall (the wall encloses the chamber into which the growth substrate is placed).

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANTA G. DOE whose telephone number is (571)270-3152. The examiner can normally be reached on Mon-Fri 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. G. D./
Examiner, Art Unit 1775

/Michael A Marcheschi/
Supervisory Patent Examiner, Art Unit 1775